Rag2 Targeted Mutation Mice from Taconic

In vivo Immunology Model for Drug Discovery and Toxicology

The Taconic Rag2 Targeted Mutation Mouse

- Lacks mature T and B lymphocytes due to an inability to initiate V(D)J rearrang-ement. Otherwise, the mouse exhibits apparently normal hematopoiesis.

Potential Applications of the Rag2 Targeted Mutation Mouse

- Evaluate function of lymphocyte specific genes in immune cell differentiation (Figure 1).
- Reconstitute with human hematopoietic cells for research in AIDS and other immune cell disorders.
- Model human hematopoiesis for studying experimental therapeutics or developing vaccines.
- Research the immune system's effect on tumorigenesis and metastasis.
- Investigate somatic cell therapy *in vivo.*
- Explore the genetics of autoimmmune or infectious diseases.

Scientific Profile of the Rag2 Targeted Mutation Mouse[1, 2]

The Taconic Rag2 Targeted Mutation Mice carry a germline mutation in which a large portion of the *Rag2* coding region is deleted. Mice homozygous for the mutation are observed to lack mature T and B lymphocytes. Analysis of these mice indicate that the *Rag2* defect blocks T cell and B cell differentiation earlier and/or more completely than the *scid* defect.

Homozygous mutant mice were found to appear normal except for immunological defects. Spleens, thymuses, and lymph nodes were small and hypoplastic. No detectable alterations were observed in other tissues tested.

Mice heterozygous for the mutation were found to be normal compared with their wild type littermates.

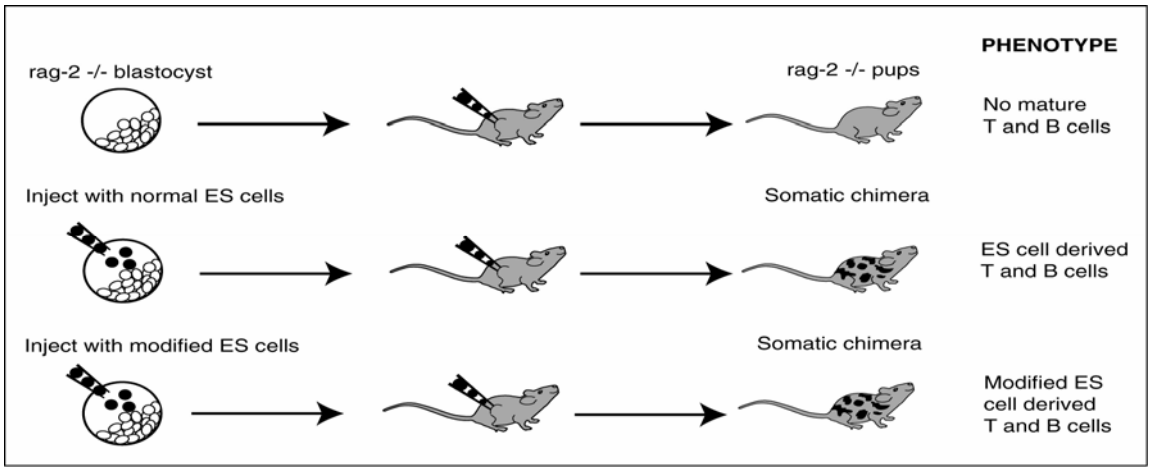

Figure 1: RAG2 deficient blastocyst complementation assay. Chen, J., Lansford, R., Stewart, V., Young, F., Alt, F. Proceedings of the National Academy of Science 90, 4528-4532. 1993. (Diagram courtesy of Dr. Chen and Dr. Alt.)

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Taconic Rag2 Mice Background Strains

Taconic Model #	Nomenclature	Background Strain	Inbred/ Congenic	Haplotype
RAG2-M	129S6/SvEvTac-*Rag2*^{tm1Fwa}	129/SvEv	Inbred	b
461-M	B6.SJL(129S6)- *Ptprc*^{a}/BoCrTac-*Rag2*^{tm1Fwa} N10	B6.SJL(129S6)	Congenic	b
601-M	C.129S6(B6)-*Rag2*^{tm1Fwa} N12	C.129S6(B6)	Congenic	d
RAGN12-M	B6.129S6-*Rag2*^{tm1Fwa} N12	B6.129S6	Congenic	b

Genetic Background

The Taconic Rag2 line is maintained on several different genetic backgrounds to meet your particular research needs (see table). The Rag2 mutant mouse on the 129/SvEv background is on the inbred strain used to create the embryonic stem cells for the initial gene targeting experiments done in the laboratory of Dr. Fred Alt. The Rag2 Targeted Mutation Mouse on the congenic B6.SJL(129S6) background makes this line useful for their identification in immunological adoptive transfer experiments.
It is similar to a C57BL/6 background except that it carries the ptprc^{a} and the pep 3^{b} genes from the SJL strain of mice. This marker is also sometimes referred to as Ly5.1.[3,4]

The Rag2 mouse is also available on C57BL/6 and BALB/c congenic backgrounds. (See above table for haplotypes.)

Origin of Models

The Rag2 mouse was developed in the laboratory of Frederick W. Alt at Columbia University. The model was created by targeting the *Rag2* gene in CCE ES cells and injecting the targeted cells into blastocysts. Ellis Reinherz of the Dana Farber Cancer Institute received Rag2 mice from the Alt lab on a mixed background. The mice were then backcrossed by S. Koyasu for 10 generations (N10) to B6.SJL-*Ptprc*^{a} (from Cancer Research). Taconic received stock in 1996. The mice were derived by embryo transfer, and the colony is maintained by mating homozygous mice.

Ready for Your Experiments

Taconic's quality program assures that each Rag2 Targeted Mutation Mouse is bred for homozygosity. Taconic mice are shipped in Taconic Transport Cages (TTC^{TM}) and come with an up-to-date health report documenting their Murine Pathogen Free (MPF^{TM}) health status. Barrier housing conditions are recommended for maintenance of Rag2 homozygous mice.

Related Mouse Models

Pfp/Rag2 (model 001177) - This double targeted mutation exhibits a severe depletion of NK cell function through the disruption of the *Pfp* gene and lacks mature T or B lymphocytes through disruption of the *Rag2* gene. It can be used to study overall regulation of the immune system or specific areas such as NK or CTL activity, immune suppression and transplantation. This mouse is homozygous for both the disrupted *Pfp* gene and *Rag2* gene. It is an alternative to traditional models bearing combinations of naturally occurring mutant genes such as the scid-bg (Prkdc^{scid}-Foxn1^{nu}) and bg-nu-xid (Lyst^{bg}-Foxn1^{nu}-Btk-^{xid}).

Rag2-HY (model 004079) - The *Rag2* gene in this model has been inactivated by homologous recombination therefore no V(D)J rearrangements can occur. The result of this manipulation allows no maturing endogenous T or B cells. This provides a background to examine the phenotypic expression of the antigen *HY* transgene. This transgene results in a large fraction of T-cells expressing an a b

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TCR specific for a minor histocompatibility antigen (H-Y) which is present on male but not female cells in the context of MHC Class I (H-2D^{b}). These mice carry an H2^{d} haplotype which is a non-selecting background for conventional T-cells. Therefore on a B10.D2 background(H2^{d}), thymocyte development is arrested at the double positive stage in both male and female *Rag2/HY* mice. These mice can be useful for studying mechanisms of self-tolerance and lineage commitment and the role of CD4 and CD 8 molecules in the deletion process of autospecific cells.

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